EDITORIAL COMMENT†

DELETERIOUS EFFECTS OF "BACTERIOPHAGE" THERAPY

Immunologists are familiar with the phenomenon of test-tube synergism between bacteria and homologous bacteriophage, the formation of a 'phage-bacterium complex of exalted pathogenicity and aggressive physiological function. Many investigators have feared that similar conjugations might take place in the animal body, which, under certain conditions, would contraindicate homologous 'phage therapy. Doctors Bronfenbrenner and Sulkin,[1] of Washington University Medical School, therefore, have rendered a valuable service to clinical research by devising a simple experimental method by means of which this fear may be tested.

In their technique, rabbits were injected intracutaneously with an arbitrary dose of low-virulent staphylococci. The rate of development and duration of the resulting local skin lesion were recorded daily in untreated and 'phage-treated animals. In their untreated controls, the local skin lesion reached its maximum size (2.5 square centimeters) by the end of twenty-four hours, and decreased to about half this size by the end of four days, and to about a quarter of the maximum by the end of seven days. Spontaneous healing was effected by the twelfth day.

In their hands, the rate of development, maximum size and rate of healing of this local staphylococcus infection were not affected either favorably or unfavorably by the continuous application of compresses moistened with nutrient broth, nor with "bacteriophage" (*i. e.*, filtered staphylococcus 'phage-lysate) prepared from low-virulent staphylococci. "Bacteriophage," prepared for virulent staphylococci, however, markedly accelerated the local spread of the experimental infection, and almost doubled the maximum size of the local lesion. The 'phage-treated lesions continued at about twice the control size for about eight days. Healing was effected by the thirteenth day.

While their demonstration of the complete absence of all beneficial effects of local 'phage therapy are applicable only to cutaneous lesions treated by moist compresses, their demonstration of a synergistic aggressive substance in certain routine 'phage-lysates is presumably of wider clinical application. They liken this synergistic aggressin to the "Reynals Spreading Factor," which can be isolated from certain animal tissues or bacterial cells.

Whether or not it is possible for the staphylo-aggressin to change a relatively unimportant local staphylococcus infection into a fatal septicemia has not yet been tested. The effects of this aggressive factor on chronic local staphylococcus infections, in which 'phage therapy is presumably complicated (or assisted?) by local allergic reactions, also has not yet been studied.

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† This department of CALIFORNIA AND WESTERN MEDICINE presents editorial comment by contributing members on items of medical progress, science and practice, and on topics from recent medical books or journals. An invitation is extended to all members of the California and Nevada Medical Associations to submit brief editorial discussions suitable for publication in this department. No presentations should be over five hundred words in length.

1 Bronfenbrenner, J., and Sulkin, S. E.: Proc. Soc. Exper. Biol. and Med., 32:1419 (June), 1935.

OBSERVATIONS ON THE TREATMENT OF MENINGOCOCCUS MENINGITIS*

Many methods for the treatment of meningitis have been promulgated in recent years, with variations in the types of serum used, and in the methods of their introduction.

Some advocate giving the serum by alternating lumbar puncture, with cisternal puncture. Some advocate through and through drainage by combining the above-named punctures, and then introducing the serum. Some advocate its use once in twenty-four hours; some in twelve, etc. One clinician uses the newly marketed meningococcus antitoxin, the next one applies manufacturer's serum, the third still another one, and so on.

Many practitioners never see over two or three cases of the disease in a lifetime of practice, and, naturally, when a case presents itself amidst all this confusion, they are more or less at sea for an exact and rational procedure.

Based on several hundred cases over a decade of experience, during which we have constantly sought for better therapy, we are happy to recommend a newer line of procedure that in all types of cases is giving us much the best results we have so far been able to achieve. Having established the diagnosis, by staining with the standardized technique, of the Gram-negative diplococcus within the neutrophiles, either from a scratch through one of the macules on the skin, or from the spinal fluid obtained by lumbar puncture, the spinal fluid is drained off and replaced with antiserum by the gravity method, to which is added 5 cubic centimeters of fresh human serum containing complement, obtained by bleeding some Wassermann-negative donor. When the specific serum fails to flow freely and easily, no more is given. Concurrently, meningococcus antitoxin is given intravenously. The latter procedure is not repeated unless the hematogenous form of the disease predominates.

A culture is promptly made from the spinal fluid, and within twenty-four hours it is tested in the laboratory against the various antisera supplied the market by the different manufacturers. Then only that brand is selected for treatment which agglutinates the living organisms in the most dilute titer, and each time it is used, the human complement is added.

The results have been most prompt and gratifying to both physician and patient. One may never predict which serum will be the one most useful, though one brand has been found to be of service far oftener than all the rest. However, where one has not the facilities for culture and agglutination, a practical procedure may be obtained in

* Article submitted on July 19, 1935.

alternating different brands of serum at each treatment, adding the complement. Experiment in these cases has shown the infected spinal fluid contains no natural complement of its own.

Puncture is done every eight to twelve hours or oftener, depending upon the pressure symptoms manifested by the patient. We prefer to alternate lumbar with cisternal. Treatment is discontinued when the patient seems sufficiently well; when the organisms disappear from the spinal fluid; and when the sugar content of the spinal fluid, as measured by drops against 5 cubic centimeters of test solution, again approaches normal. Overtreatment is very deleterious. If relapse or undertreatment is feared after discontinuing spinal therapy, the patient may be kept desensitized for a suitable period by giving a small dose of serum in the muscle every fourth day. We have observed much better results with the above procedure in all types of cases of any severity than in similar cases treated by previous methods, either with antiserum alone, or antitoxin alone.

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Air Conditioning at University of California Hospital.—The air-conditioned room at the University of California Hospital, which seems to have solved a number of the problems surrounding the transmission of the common cold, has been made the subject of a special article in *The Aerologist,* a national publication devoted to air conditioning. The article describes in detail the attempts of the University physicians to have a number of selected subjects "catch cold" in the air-conditioned room without avail. Twenty-eight chronic cold sufferers were placed in the room during the experiment and subjected to many sure-fire methods of contracting their favored complaint. But none did. The only special treatment given them was purified air scientifically circulated at a constant temperature of 70 degrees.

The room, with bed space for from four to six patients, is completely isolated from the outside atmosphere. An air lock keeps the outside air down to the necessary minimum, and there are other devices which provide for a continuity of service to patients without disturbing the atmospheric conditions within the room.

The subjects treated were all males between the ages of twenty-one and forty-nine years, and each having an average of five or six colds a year. They were kept in the room for a sufficient period to free them of all traces of the ailment and then a person suffering from a cold was brought in. The others were allowed to play cards with him, drink from the same glass, and do many other things to coax the cold germs into their own systems. At the end of the experimental period not one single case of cold had been transferred.

Two representatives of the University of California, B. F. Raber, professor of mechanical engineering, and Prof. H. B. Walker of the Branch of the College of Agriculture at Davis, were in attendance at the National Homes Conference at Purdue University, where they reviewed the elaborate plans of that university to experiment with a group of ten to twenty moderately priced homes to be constructed on a plot of land near the campus. Professor Raber also spoke at the meeting on the advances being made by air conditioning in California.

The man who has not anything to boast of but his illustrious ancestors is like a potato—the only good belonging to him is underground.—Sir Thomas Overbury.

ORIGINAL ARTICLES

THE MEDICINAL TREATMENT OF HEPATIC AND BILIARY DISORDERS*

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IN the treatment of hepatic and biliary disorders by means of drugs, one may have several laudable desires, namely, to relieve pain, to relieve or avoid stasis by emptying out the bile reservoirs, to increase the bile flow for the purpose of cleansing the bile passages, and to disinfect or to inhibit bacterial growths within the bile tract. Obviously, varying degrees of success may be expected in these endeavors. In spite of the apparent apathy of most practitioners of medicine toward several of these aims, pharmacologists continue to study substances that may be so employed, and experimental physiologists and pathologists occasionally remind the clinicians that they may profit by the new discoveries more actively and efficiently.

Substances that have been used for their effect upon the liver and bile passages are legion. Foods as well as drugs are included in this category. The German literature of the past year contains many references to studies on plants, as cholagogues, and many of the plants so listed are used also as food. Indeed, under normal conditions, the effect of foods constitutes one of the important sources of stimulation of the physiological processes to be discussed. Von Bergmann classifies these substances under five different headings: (1) Cholekinetica, means used to set in motion the extrahepatic biliary mechanism; (2) choleretica, means used to affect the secretion of the liver; (3) antispasmodica, substances used to diminish the heightened tonus of the smooth musculature; (4) antineuralgica, for the relief of pain; and (5) antiphlogistica, to combat bacteria and inflammation. A glance at Table 1, modified from that of von Bergman, will give an idea of some of the materials offered for use.

Lauda remarks that a distinction between choleretics and cholekinetics is not a particularly practical one, since most choleretics are also cholekinetics and most cholekinetics are also choleretics. But the experimental work of the past decade seems to lend weight to the distinction. There is no doubt concerning the pharmacological value of some of these materials, to wit, bile salts as choleretics; oils, fats, peptone, and pituitrin as cholekinetics; belladonna and its derivatives as antispasmodics; and the opiates as analgesics. They are of proved potency and of sufficiently low toxicity. The stumbling-block is encountered in the clinical indications for their employment.

Permit me to quote two contrasting statements. In the recent tenth edition of the "Textbook of Pharmacology and Therapeutics" by Cushny, thoroughly revised by Edmunds and Gunn, it is

* Guest-speaker paper. Read before the general meeting of the California Medical Association at the sixty-fourth annual session, Yosemite, May 13–16, 1935.